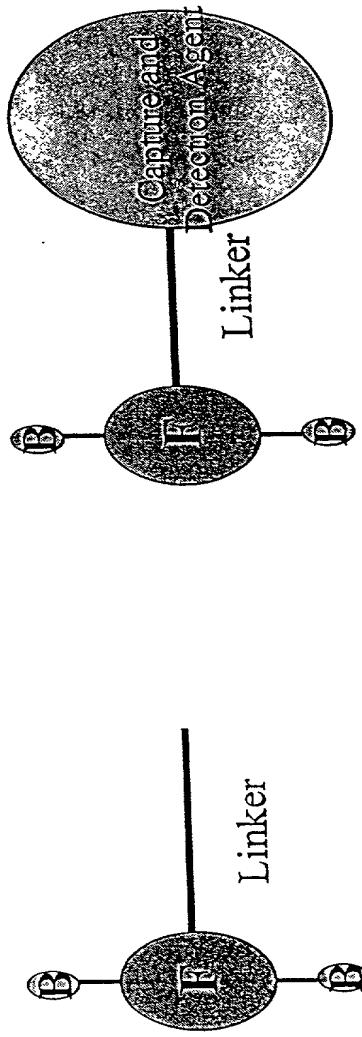


## High-throughput Target ID



## Library of Bioactive Compounds

## Library of Target ID Compounds

Use corresponding activity-based probe to identify the biological target

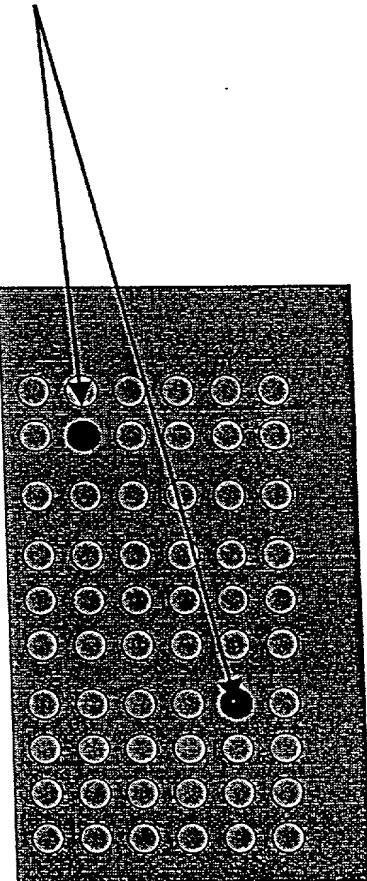
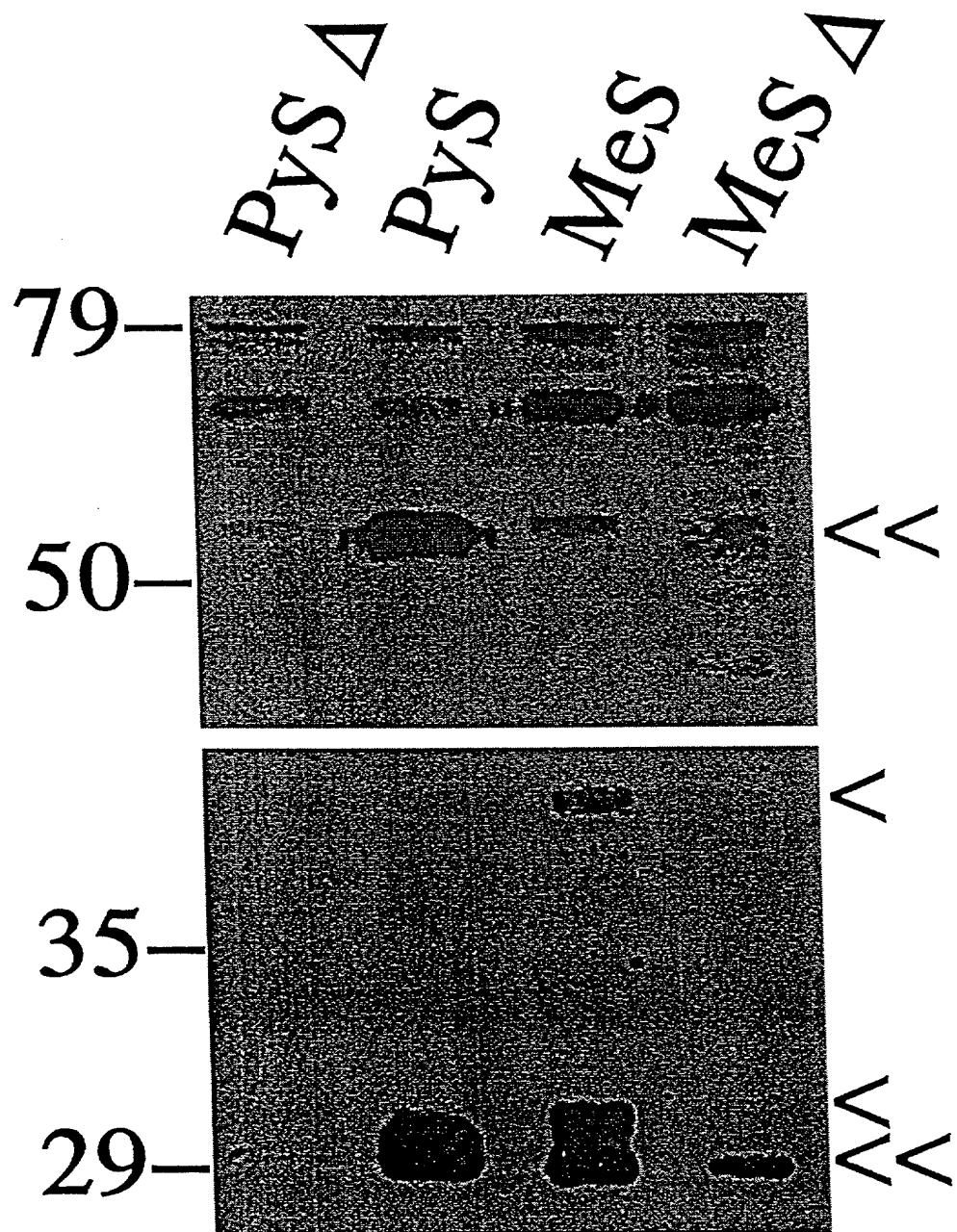


FIGURE 1

FIGURE 2



# Non-Directed Tagged Library of Sulfonates Identifies Probe for ADH Superfamily of Enzymes

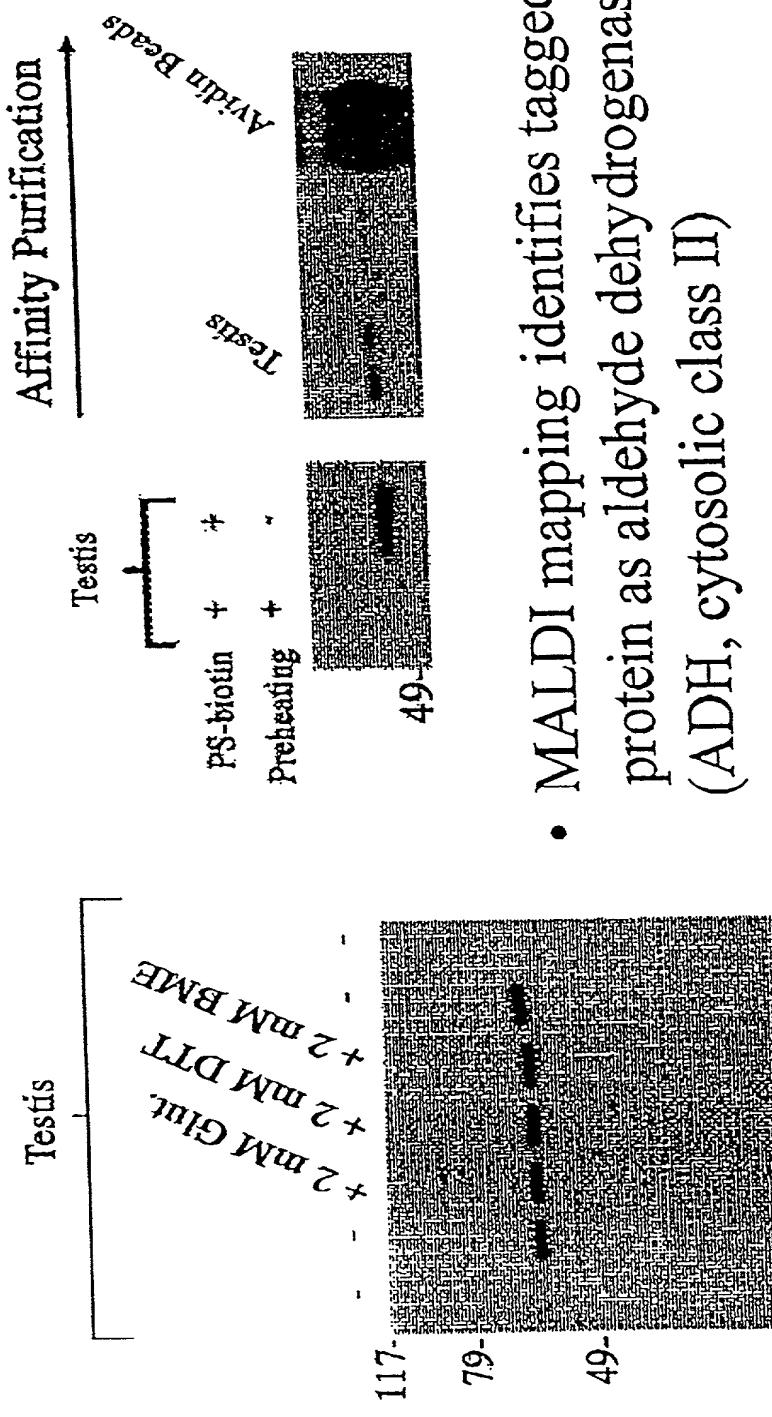
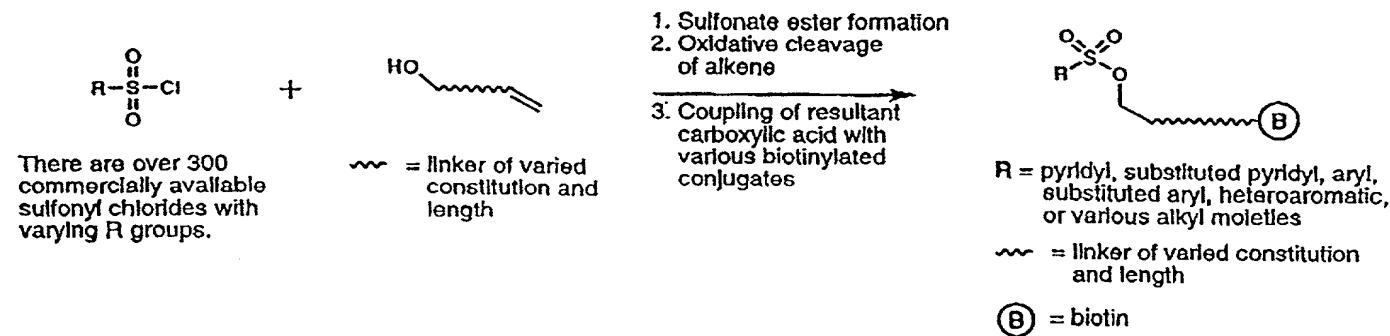


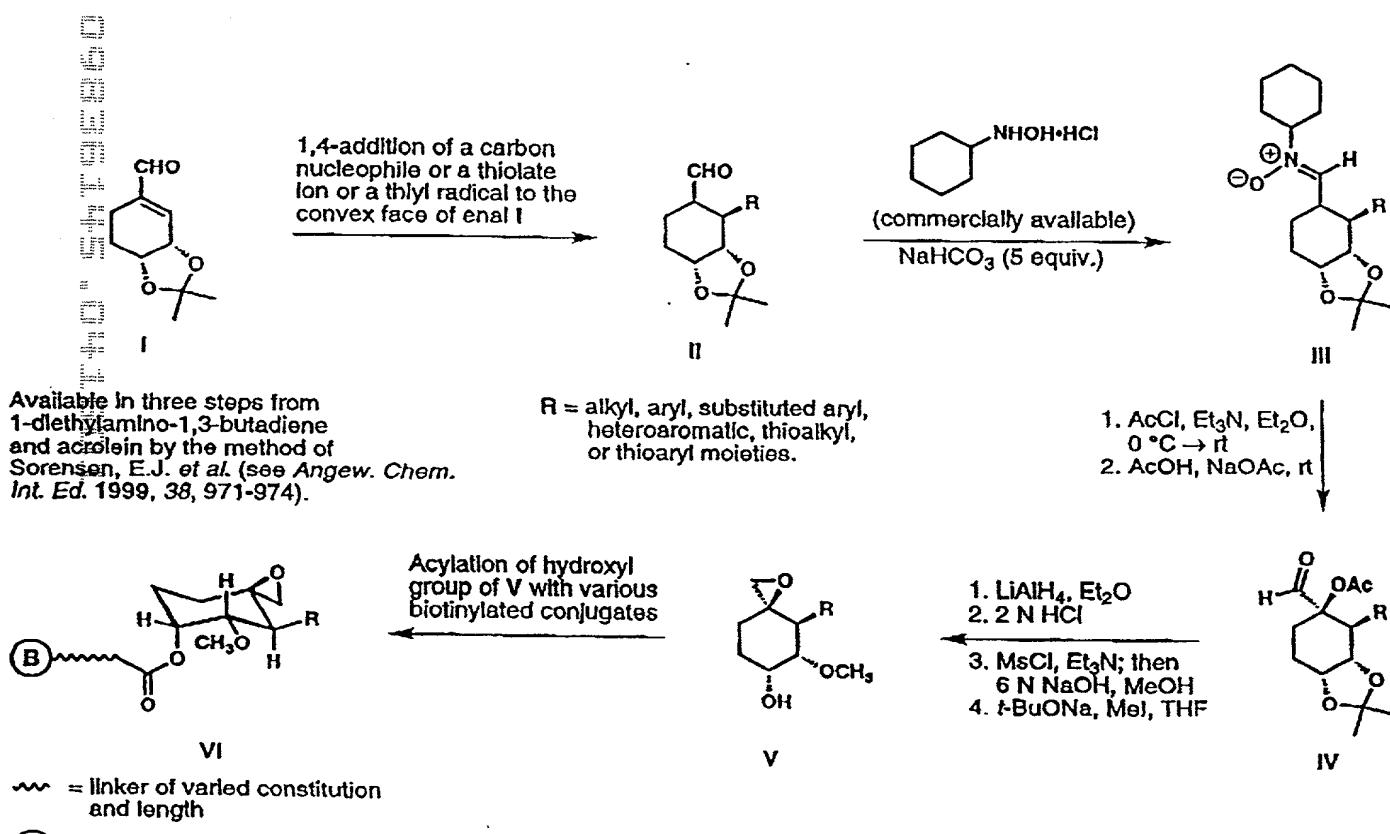
FIGURE 3

- MALDI mapping identifies tagged protein as aldehyde dehydrogenase (ADH, cytosolic class II)
- 28 ADHs in fly genome
  - Involved in retinoic acid biosynthesis and catabolism of alcohol and chemotherapeutic agents

FIGURE 4



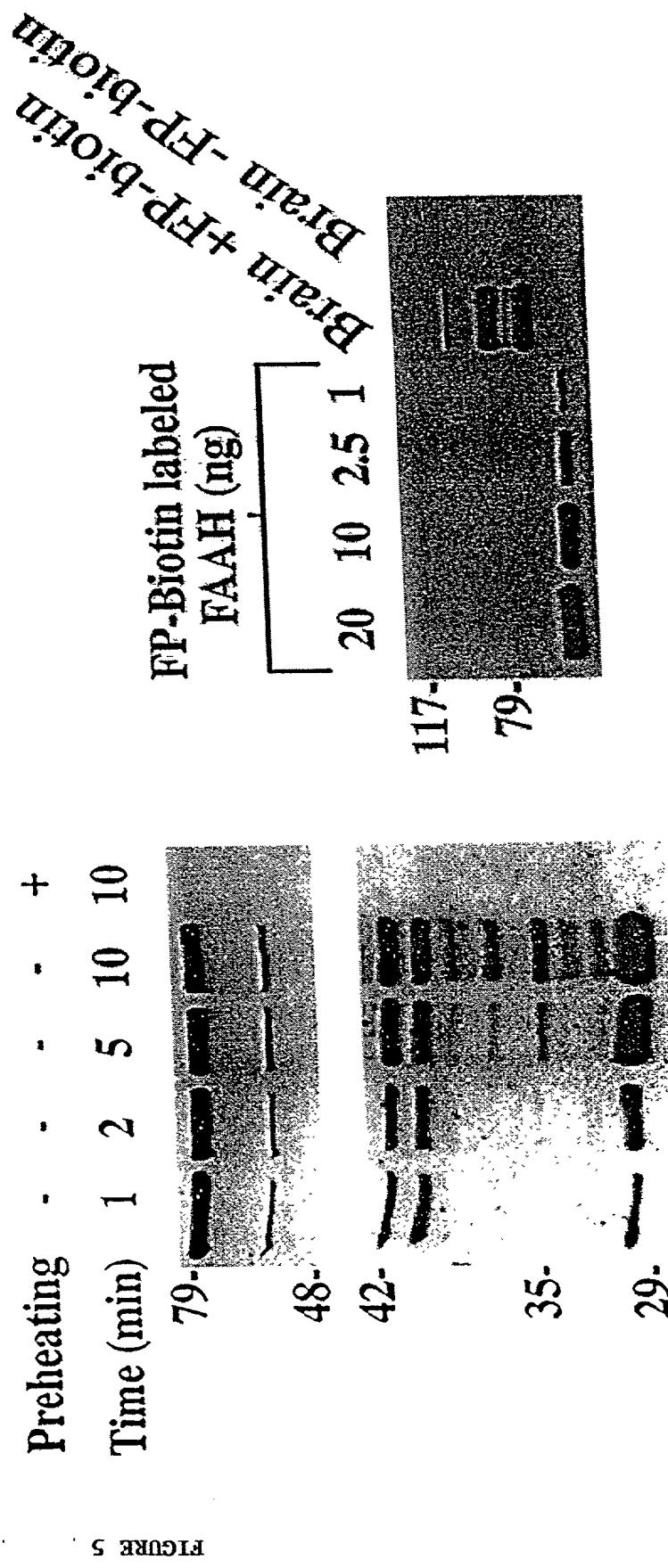
Scheme 1. A pathway for syntheses of various biotinylated sulfonate esters for use in activity-based proteomics studies.



Scheme 2. A strategy for convergent, stereocontrolled syntheses of conformationally well-defined spiroepoxides of type VI. Literature precedent for I → II → III → IV → V can be found in Sorensen, E.J. et al. *Angew. Chem. Int. Ed.* 1999, 38, 971-974. Compounds of type VI are analogs of the metalloprotease (MetAp-2) inhibitor fumagillin and will be employed as covalent affinity agents in activity-based proteomics studies.

## FP-Biotin: a kinetic reporter of SH Activity

- The rates at which the majority of SHs react with FP-biotin can be experimentally followed
- FP-biotin readily detects low femtomole quantities of SHs directly in complex cell/tissue proteomes



Utility of Multiplexed probes in identifying  
Serine Hydrolases

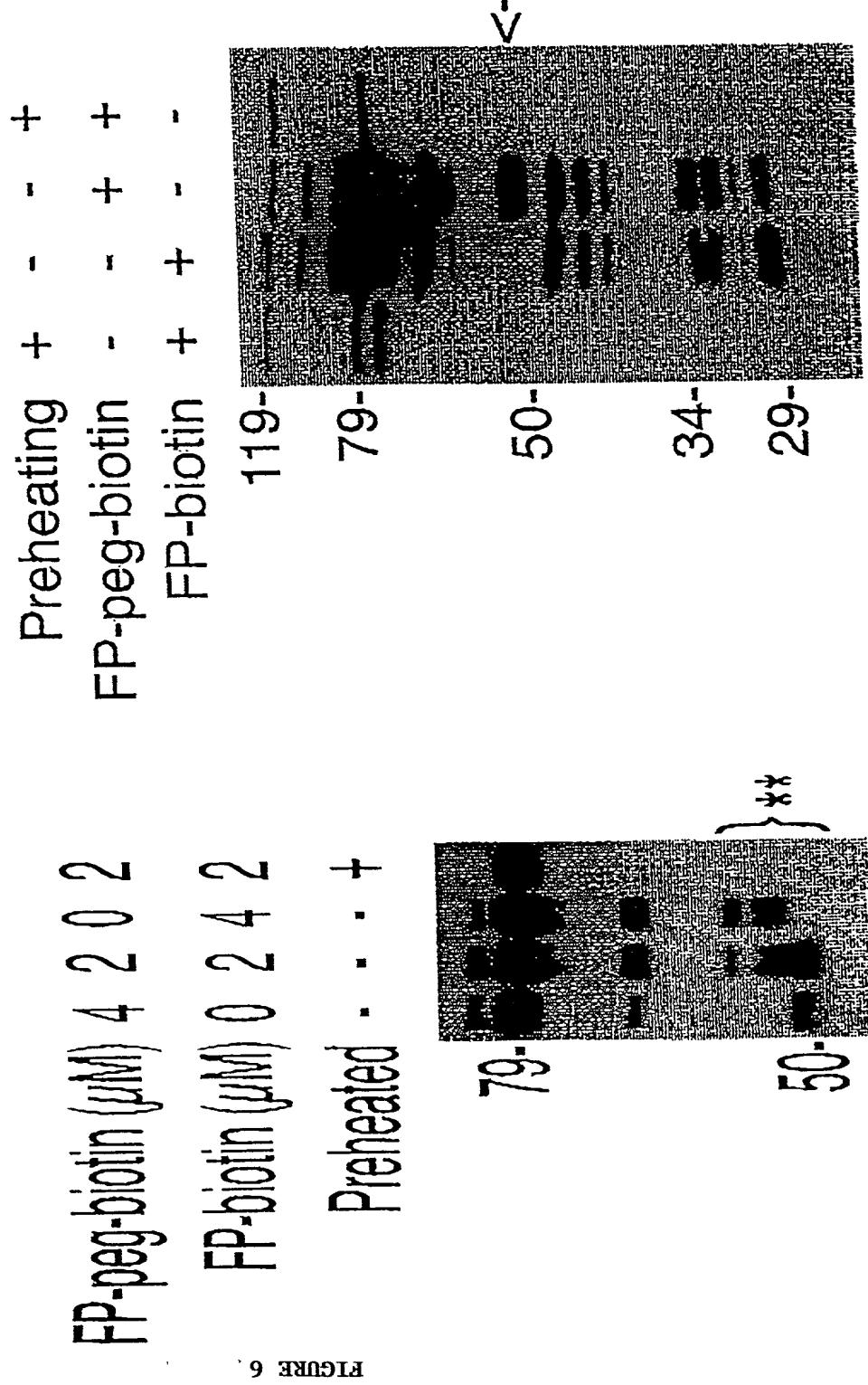


FIGURE 7

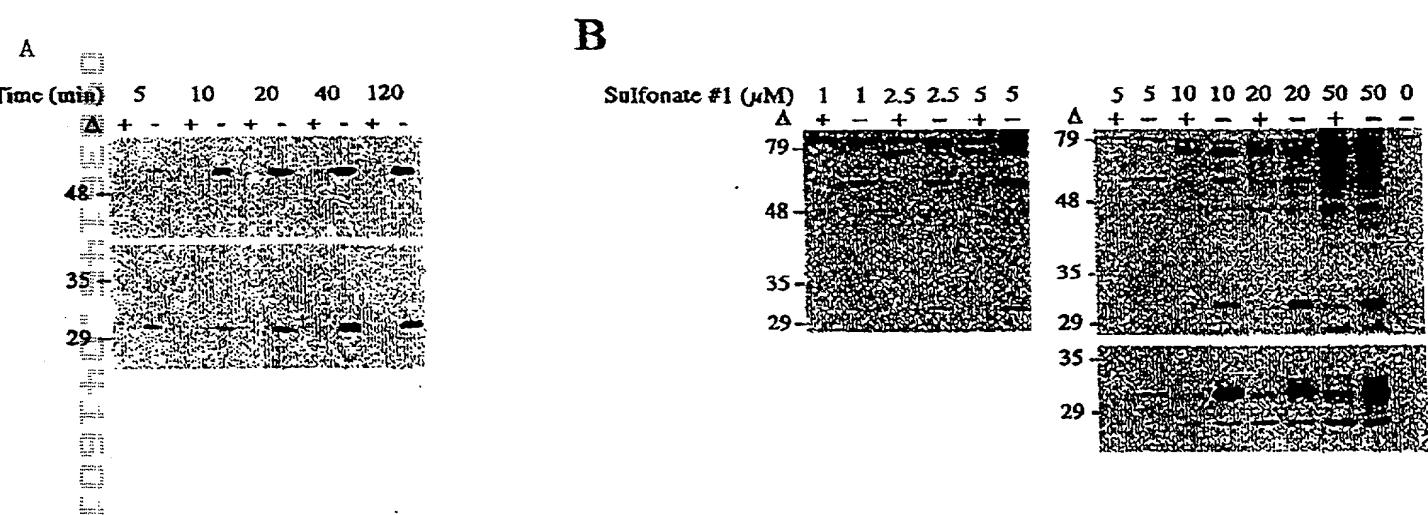
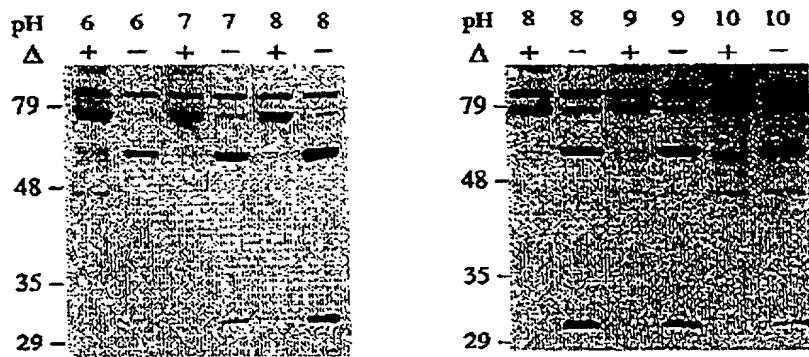


FIGURE 7

C



D

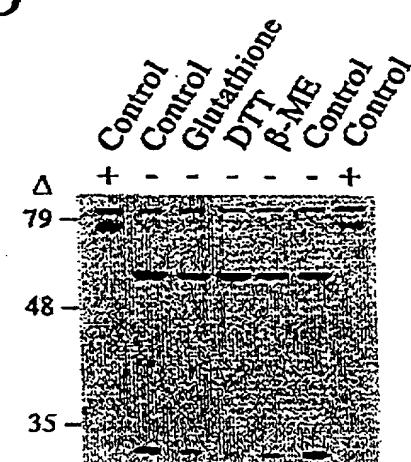


FIGURE 8

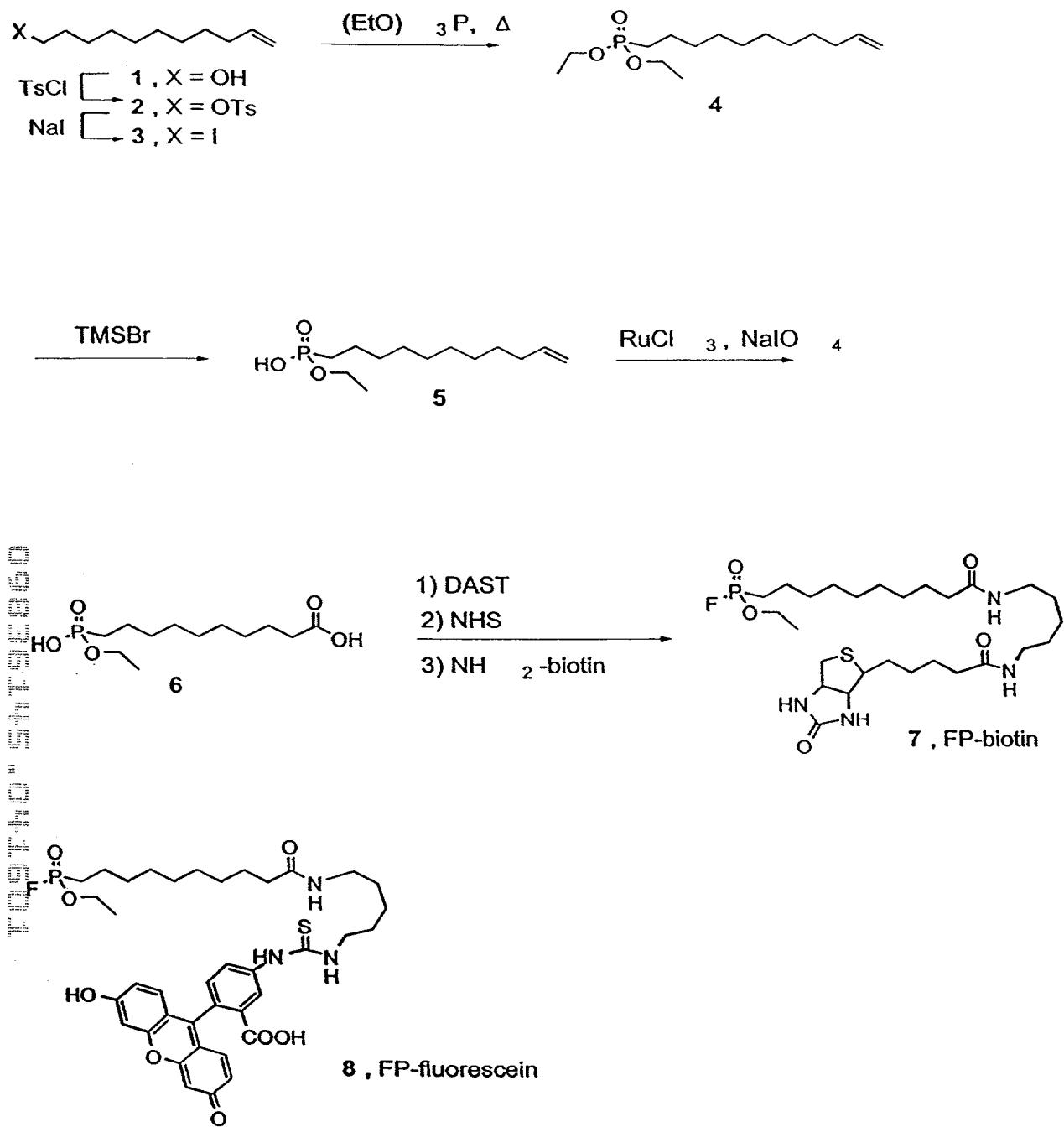


FIGURE 9

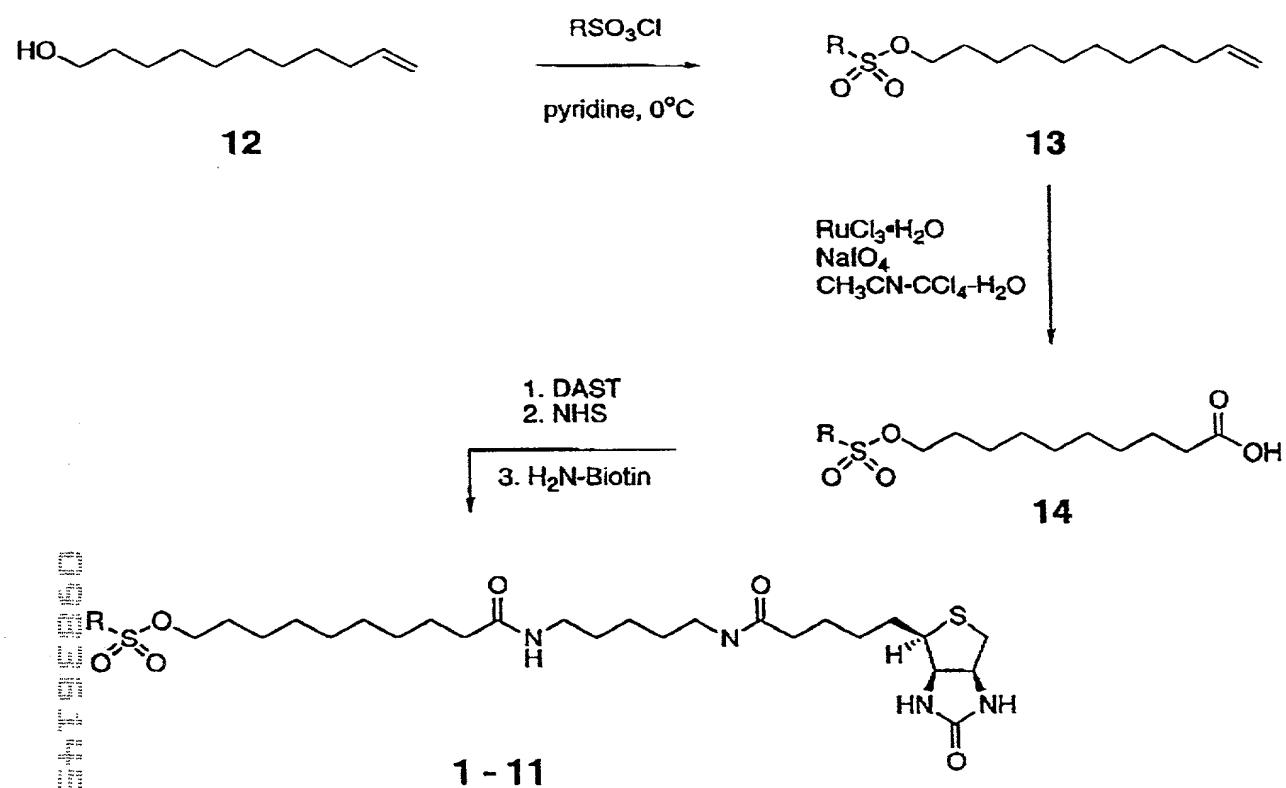
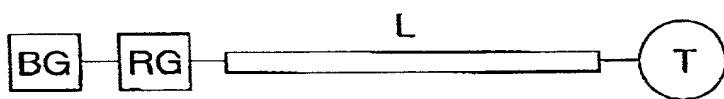


FIGURE 10

A.



B.

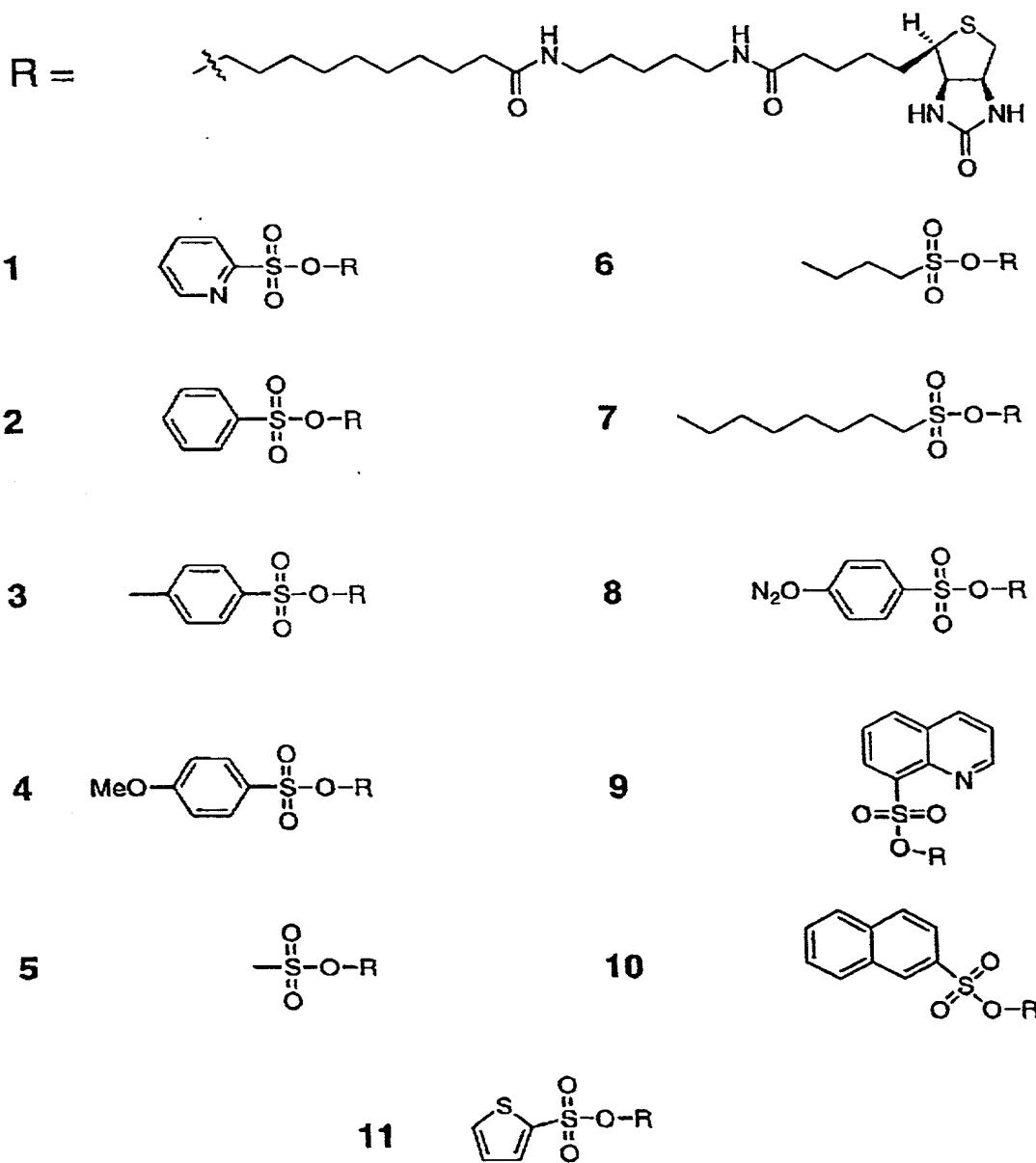
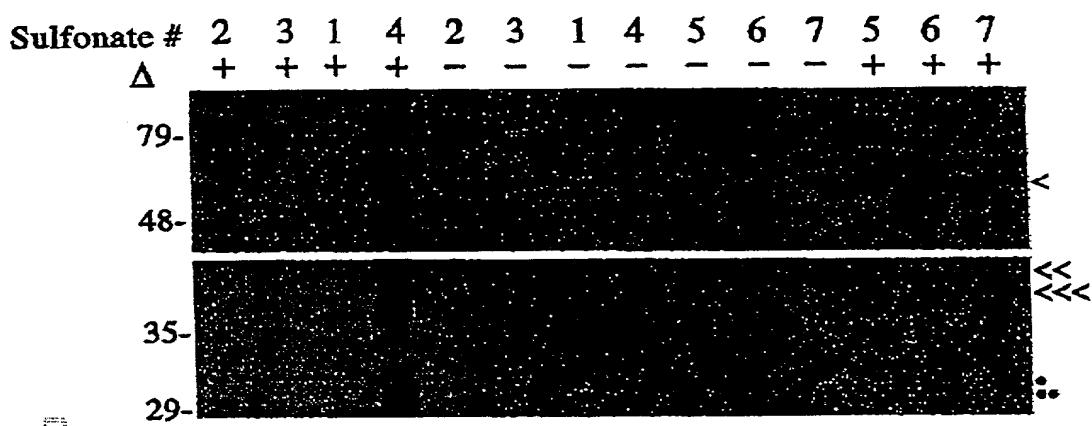


FIGURE 11

A



B

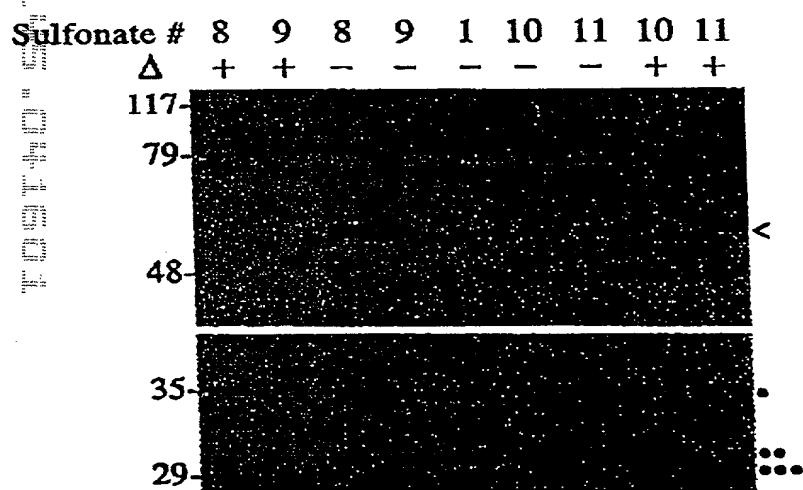


FIGURE 12

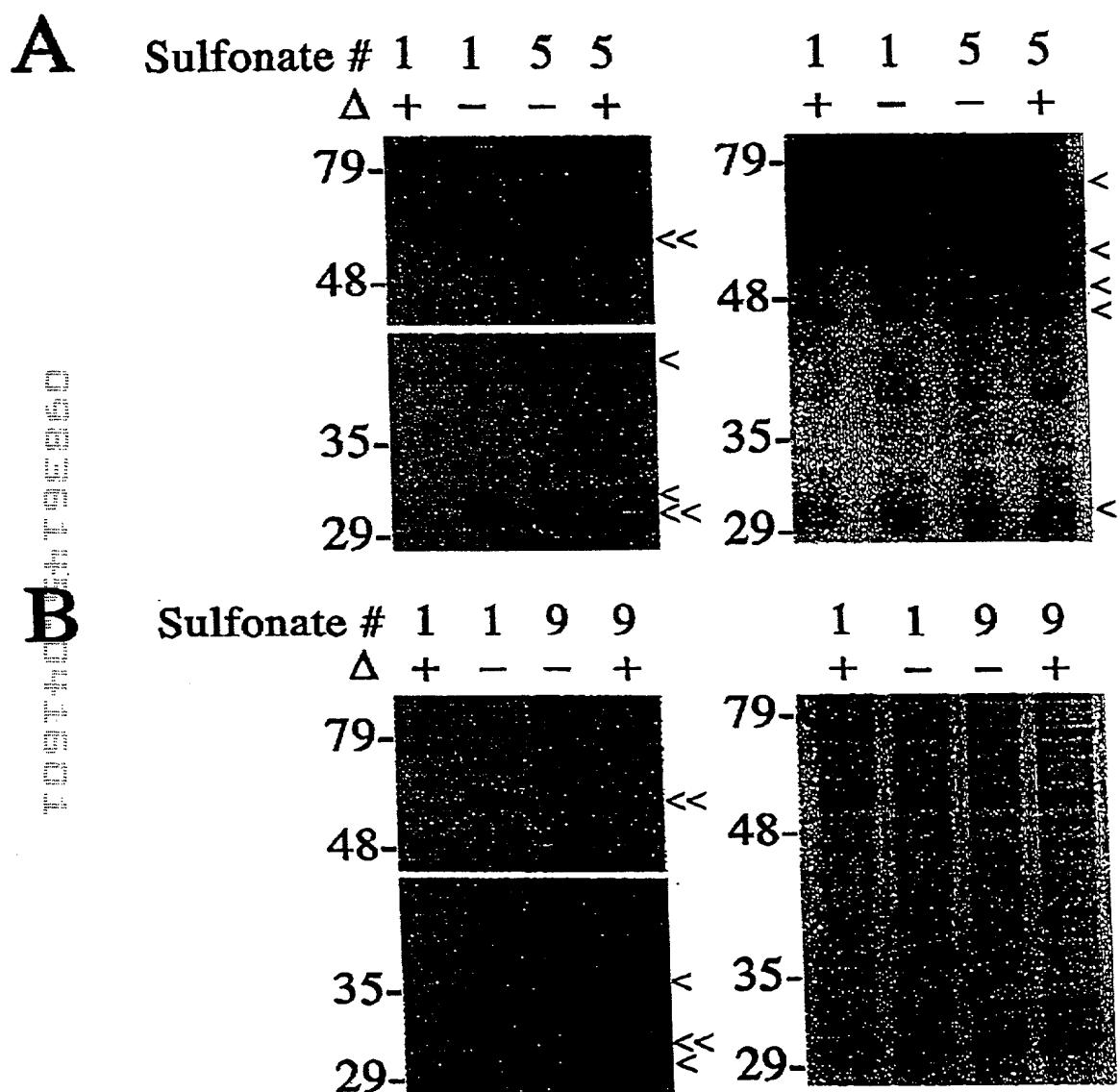
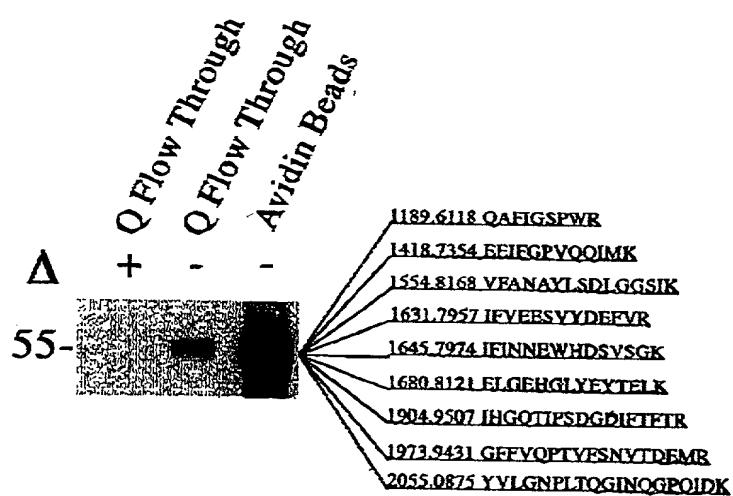
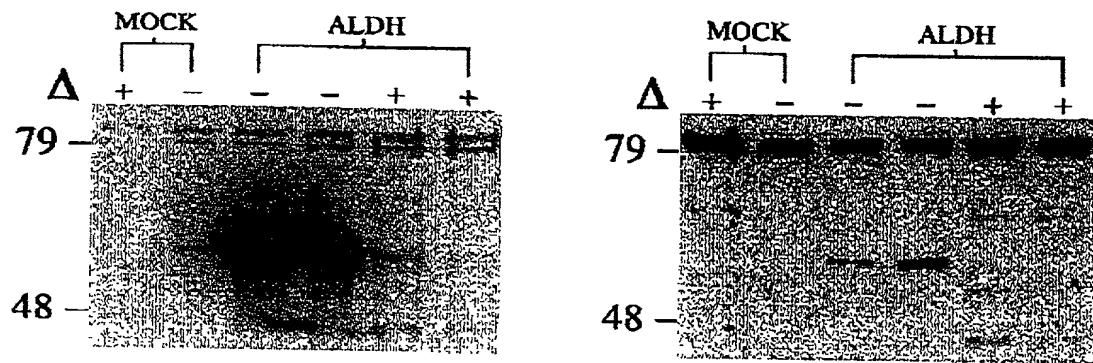


FIGURE 13

A



B



C

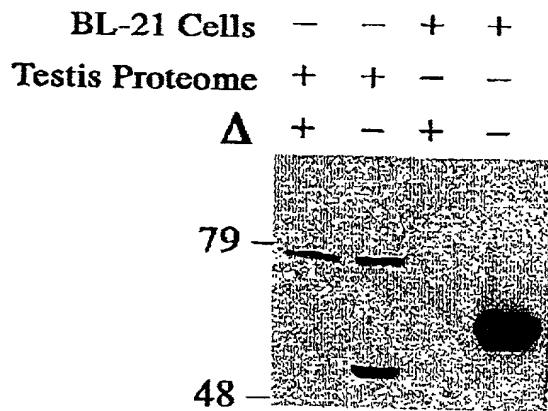
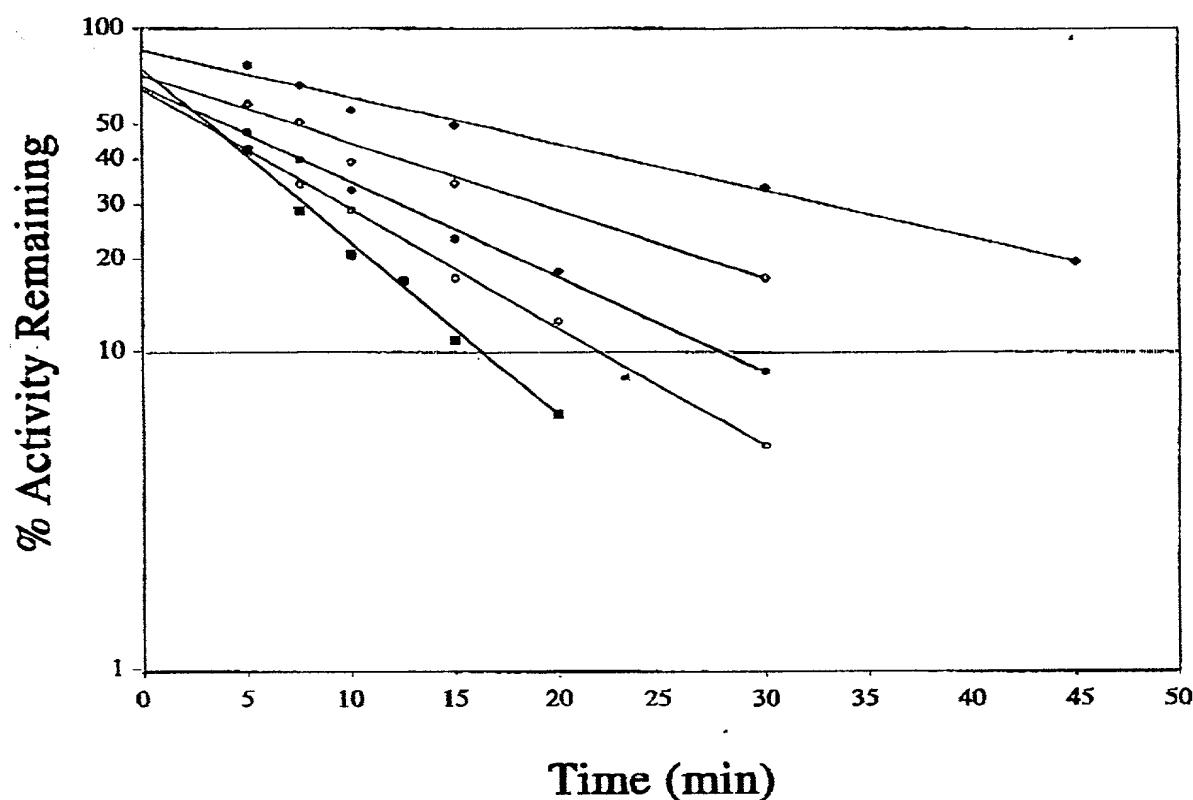


FIGURE 14

A



B

Competitor #	-	-	15	17	16	15	17	16
[Competitor ( $\mu$ M)]	0	0	5	5	5	50	50	50
$\Delta$	+	-	-	-	-	-	-	-

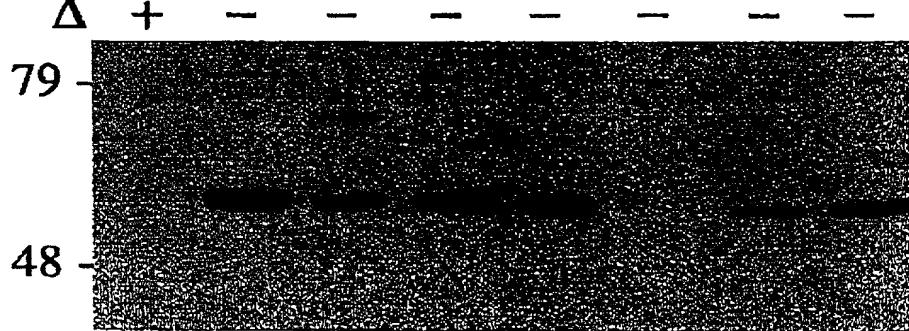


FIGURE 15

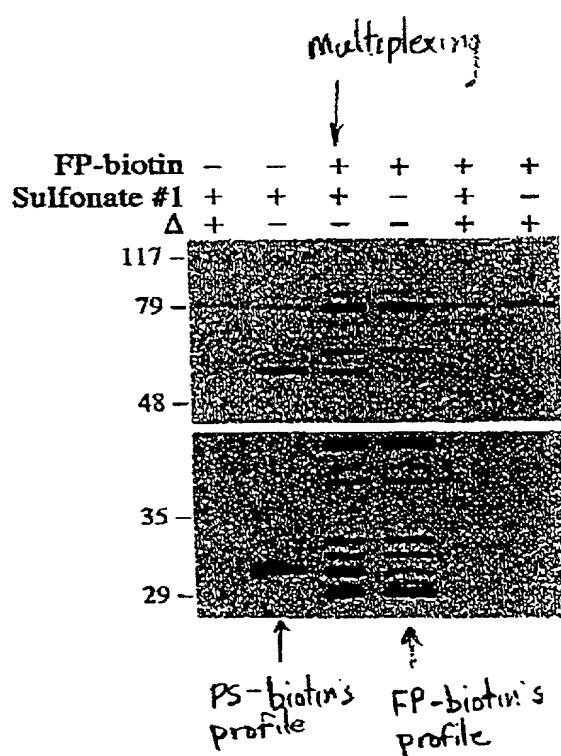


FIGURE 16

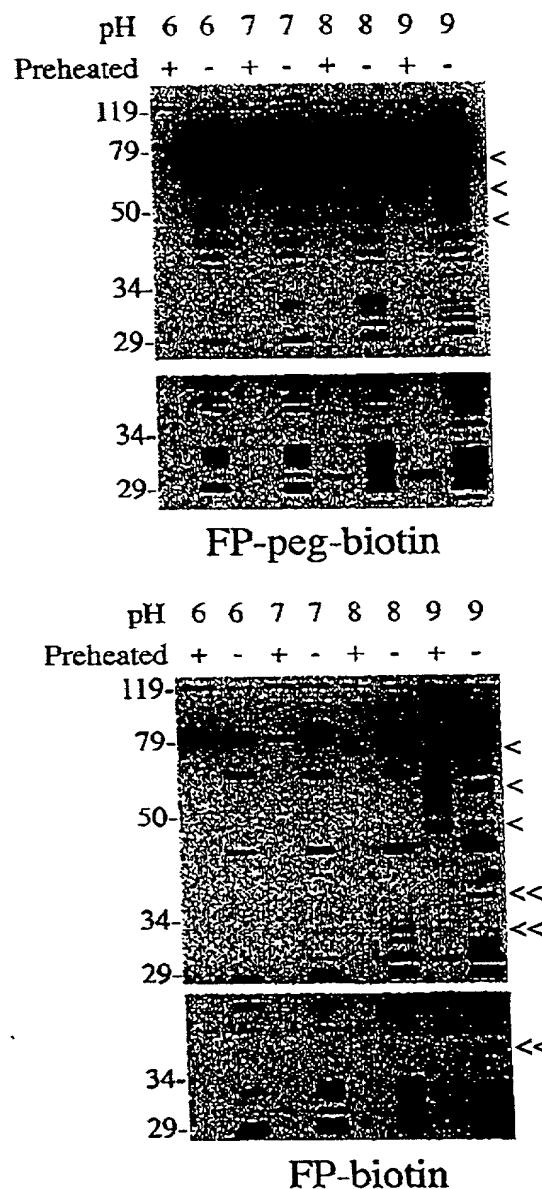


FIGURE 17

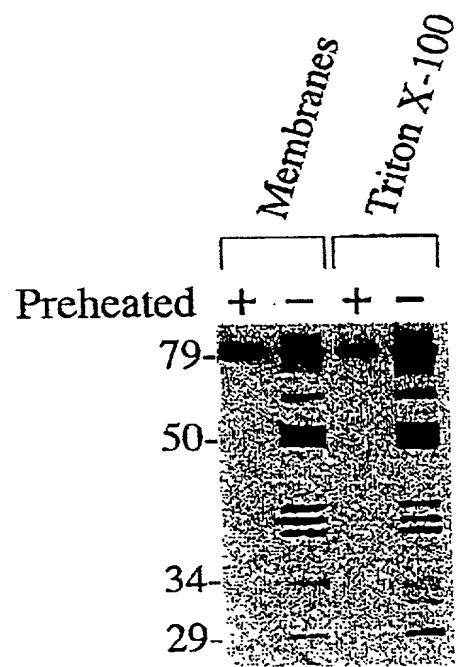


FIGURE 18

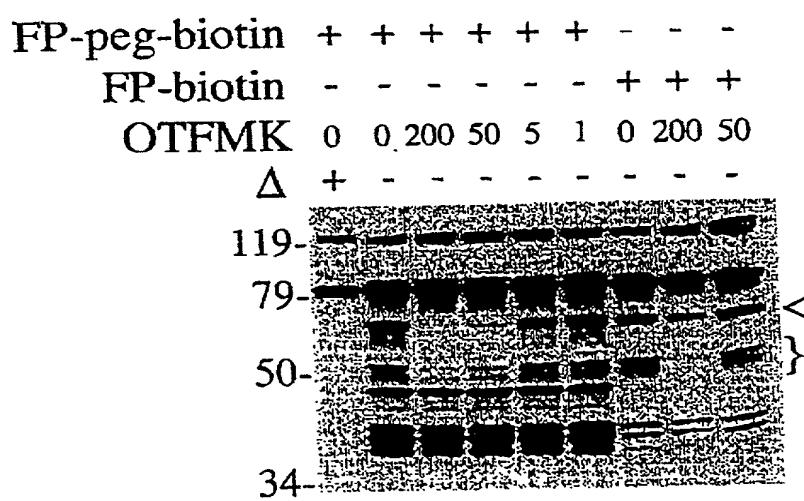


FIGURE 19

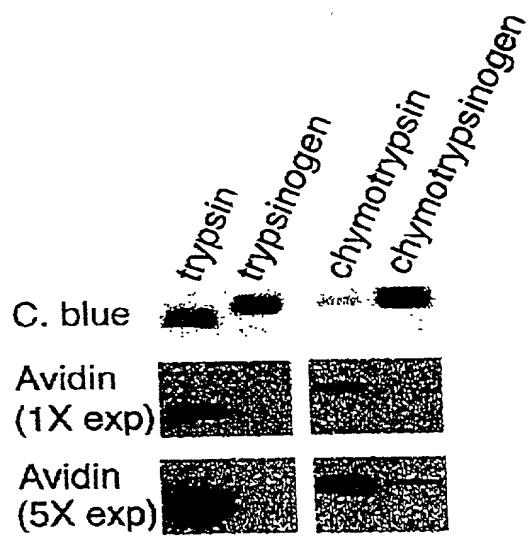


FIGURE 20

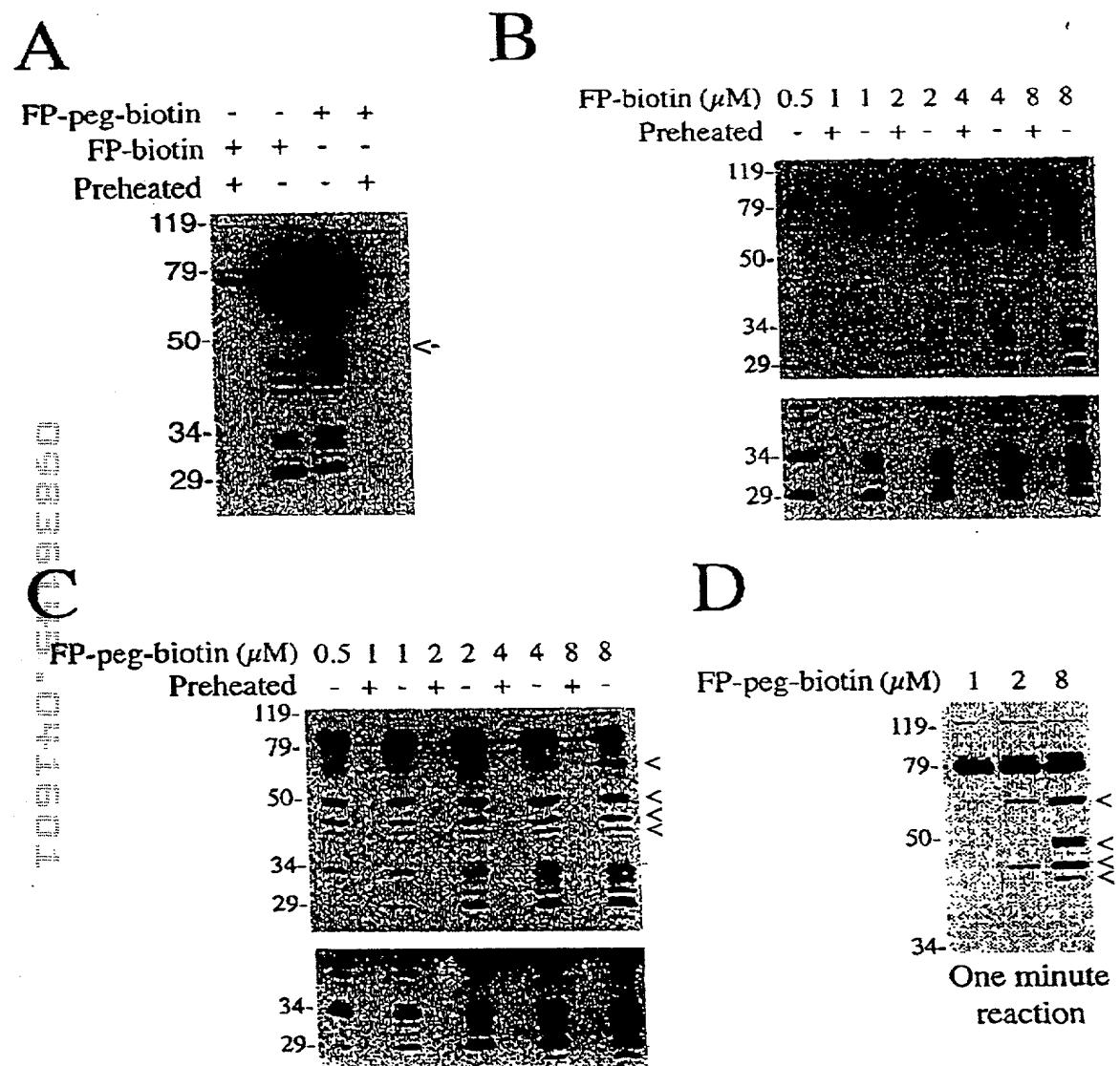


FIGURE 21

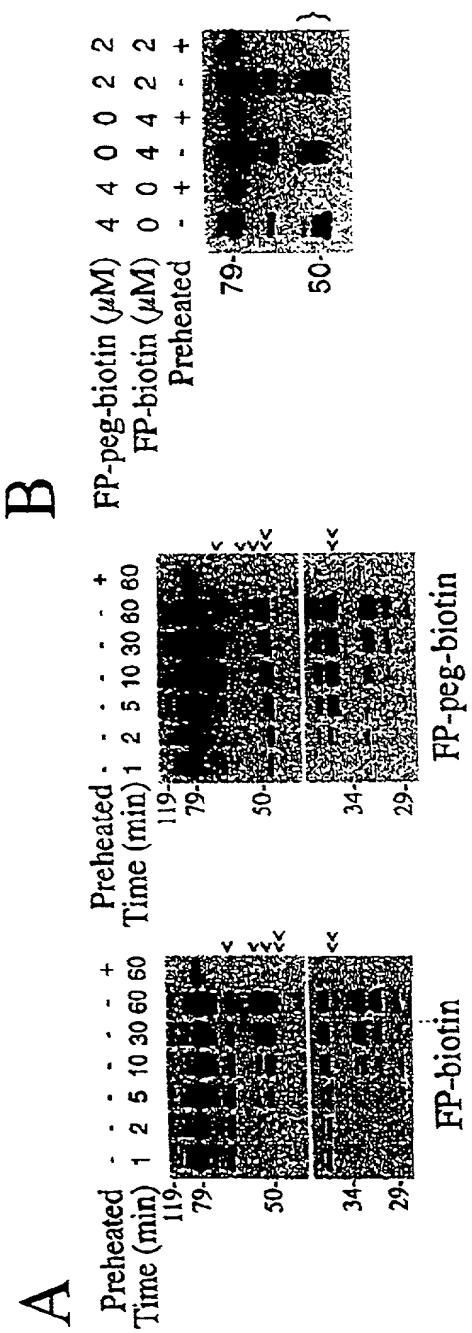


FIGURE 22

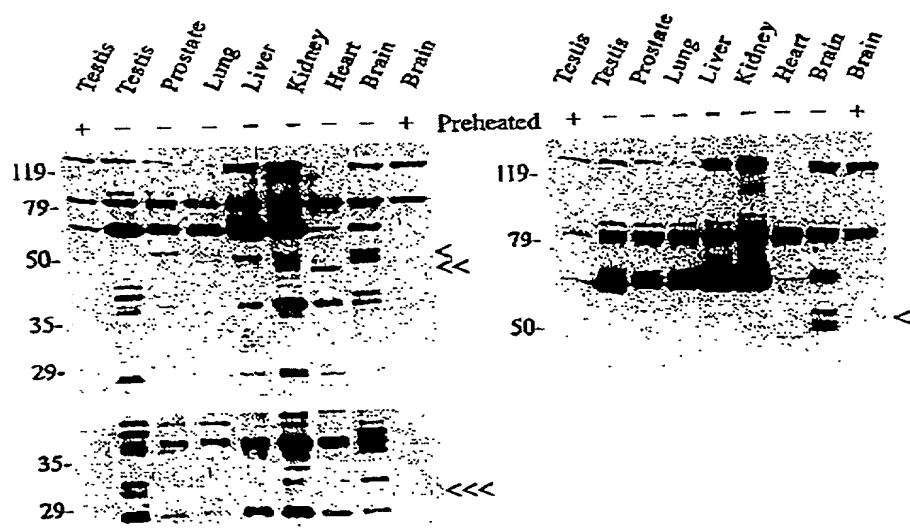


FIGURE 23

